REMARKS

Claims 1-15 and 17-20 are pending in this application. Claims 1-12 and 18-20 stand rejected and claims 13-15 and 17 were withdrawn from consideration. Reconsideration and allowance of the claims is respectfully requested in view of the following remarks. Applicants also wish to draw to the Examiner's attention co-pending application US Application No. 11/579,675 which application is titled "Antisolvent Emulsion Solidification Process."

REJECTIONS UNDER 35 U.S.C. § 103(a)

Claims 1-3, 5-8, 10 and 16 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Jakupovic et al. (US Patent 6,221,398) in view of Subramaniam et al (US Patent No.: 6,113,795). Applicants traverse this rejection for the reasons provided herein below.

This instantly claimed process provides a continuous antisolvent solidification process where a liquid medium comprising at least one dissolved organic or inorganic compound is introduced through a membrane into one or more antisolvents, or vice versa. Continuous operation is achieved by introducing the liquid medium comprising at least one organic or inorganic compound into the antisolvent(s) by forcing it through a membrane which is positioned in a membrane module (or visa versa), where the membrane has up to 3 μm pores and the shape of the membrane is selected from tubes, fibres, or spiral wounds (see, e.g. page 16, lines 17-21).

In contrast, Jakupovic et al relates to a batch process for producing pharmaceutical powder for inhalation which comprises crystalline particles of an inhalation compound. In Jakupovic et al an inhalation compound is dissolved in a solvent, the solution containing the inhalation compound is then introduced in droplet form or as a jet stream into an antisolvent which is miscible with the solvent and which is under agitation, under non-supercritical conditions (see column 2, lines 26 to 34 of Jakupovic et al). The solution is introduced into the antisolvent, for example, through a porous filter or one or more nozzles (see column 2, lines 63 to 65). Exemplified are batch-type preparation processes which use Pyrex Glass Filters having pores of 10 to 160 microns (column 4, lines 24 to 27). Jakupovic et al does not to teach or suggests to the skilled artisan modification of the batch process to arrive at the claimed continuous process. In addition, Jakupovic et al does not teach or suggest that Pyrex Glass Filters can be easily exchanged for a membrane. As noted by the Examiner,

Jakupovic et al does not teach a membrane having 3 um pore size and shaped as tubes, fibres, and spiral wounds. Accordingly, Jakupovic et al does not render the claimed invention obvious.

The instantly claimed process provides an improved antisolvent solidification process which does not have the disadvantages of a batch crystallization process (see, e.g. page 20, lines 12-16, of the specification). In particular, the instantly claimed process can be easily scaled up for commercial production while maintaining robust control of the particle size (see page 5, lines 19-21, of the specification). The instantly claimed continuous process allows for the ratio of solvent to antisolvent to be controlled thereby resulting in more uniform particle size (see, e.g page 5, lines 6-21, page 15, lines 17-19 and page 20, lines 12-23). In a batch process, such as Jakupovic et al , the ratio of solvent to antisolvent varies and accordingly, so will the particle size.

Subramaniam et al does not remedy the deficiencies of Jakupovic et al . Subramaniam et al relates to a process for harvesting particles wherein the desired particles are retained by the filter while the solvent and most of the antisolvent pass through the filter resulting in separation of the particles from the solvent (see Subramaniam et al abstract). In Subramaniam et al the drug containing solution and antisolvent are simultaneously introduced into a precipitation chamber (see column 6, lines 1-14). The effluent from the crystallization chamber is transported to a high pressure separation vessel containing a membrane (see column 6, lines 15-40) which retains the drug but not the solvent. Accordingly, Subramaniam et al, either alone or in combination does not render the claimed process obvious. Withdrawal of this rejection is respectfully requested.

Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Jakupovic et al in view of Subramaniam et al and further in view of Nocent et al.(*J. Pharm. Sci*, 90, 1620-1627). Applicants traverse this rejection for the reasons provided herein below.

For the reasons stated herein above Jakupovic et al and Subramaniam et al, either alone or in combination, do not render the claimed process obvious. Nocent et al relates to the type of solvent, antisolvent and emulsifier and the concentration of the emulsifier for the production of spherical crystals of salbutamol sulfate (see, abstract). Nocent et al does not does not teach or suggest a continuous antisolvent solidification process where a liquid medium comprising at least one dissolved organic or inorganic compound is introduced

through a membrane in a membrane module into one or more antisolvents, or vice versa. Accordingly, Nocent et al does not remedy the deficiencies of either Jakupovic et al or Subramaniam et al. Withdrawal of this ground of rejection is respectfully requested.

Claims 1, 8 and 9 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Jukapovic et al in view of Sabramaniam et al and in view of Chen et al (US Patent 7,374,779) as evidenced by Nakagawa et al. (*Japan J. Pharmacol.* 29, 509-514, 1979). Specifically the Examiner alleges that Chen et al cures the deficiency of Jakupovic et al and Subramaniam et al by teaching a process for forming progesterone or 3-ketodesogestrel crystal particles. Applicants traverse this rejection for the reasons provided herein below.

Chen et al relates to pharmaceutical formulations and systems for improved absorption and multistage release of active agents. Chen et al generally discusses a variety of techniques for manufacturing the active agent, including crystallization by dissolution in appropriate solvents (see column 54, lines 35-37). The primary focus of Chen et al is formulations and systems for improved absorption of agents. Chen et al does not teach or suggest a a continuous antisolvent solidification process where a liquid medium comprising at least one dissolved organic or inorganic compound is introduced through a membrane in a membrane module into one or more antisolvents, or vice versa. Such a teaching is found only in the instant application. Thus, Chen et al fails to cure the deficiencies of either of Jakupovic et al and Subramaniam et al. Accordingly, either alone or in combination, Chen et al does not render the claimed invention obvious.

Nakagawa et al relates to anti-inflammatory action of progesterone in a rat model. Nakagawa et al does not teach or suggest a a continuous antisolvent solidification process where a liquid medium comprising at least one dissolved organic or inorganic compound is introduced through a membrane in a membrane module into one or more antisolvents, or vice versa. Accordingly, Nakagawa et al either alone or in combination does not render the claimed invention obvious.

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Jukapovic in view of in view of Sabramaniam et al and Maruyama et al (US Patent 5,512,092,). Specifically, theExaminer alleges that it would have been *prima facie* obvious to modify the teachings of Jakupovic et al and Subramaniam et al. by coating the solid particles, because Maruyama teaches coating pharmaceutical solids utilizing drug coating materials. Applicants traverse this rejection for the reasons provided herein below.

Maruyama et al relates to a method for preparing an aqueous emulsions for coating solid pharmaceutical preparations. In Maruyama an emulsified stock solution is concentrated by removing a part of the liquid components while passing it through a membrane for ultrafiltration (see Maruyama et al abstract). Maruyama et al does not teach or suggest a continuous antisolvent solidification process where a liquid medium comprising at least one dissolved organic or inorganic compound is introduced through a membrane in a membrane module into one or more antisolvents, or vice versa. Thus the teachings in Maruyama fail to cure the deficiency in the teachings of Jakupovic as described above.

Claims 1, 18 and 19 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Jukapovic in view of in view of Sabramaniam et al and Siam et al (US Patent 6,851,166). Specifically, the Examiner contends that it would have been *prima facie* obvious to modify the teachings of Jakupovic et al and Subramaniam et al. by preparing the dosage in the form of tablets because Saim et al teaches that such particles can be prepared in the form of tablets. Applicants traverse this rejection for the reasons provided herein below.

Saim et al relates to a method of small particle precipitation wherein the solute partyicles are precipitated from a pressurized gaseous fluid or solution or a liquid solution and retained and dispersed in a carrier. Saim et al does not teach or suggest a continuous antisolvent solidification process where a liquid medium comprising at least one dissolved organic or inorganic compound is introduced through a membrane into one or more antisolvents, or vice versa. As Saim et al does not remedy the deficiencies of the cited reference, Saim et al does not render the claimed invention obvious. Withdrwal of this rejection is respectfully requested.

CONCLUSION

It is believed that claims are now in condition for allowance, early notice of which would be appreciated. If any outstanding issues remain, the examiner is invited to telephone the undersigned at the telephone number indicated below to discuss the same. In the event the United States Patent and Trademark Office determines that an additional extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with this filing to Deposit Account No.: 50-4205 ; Reference Number: 2003.817USD1.

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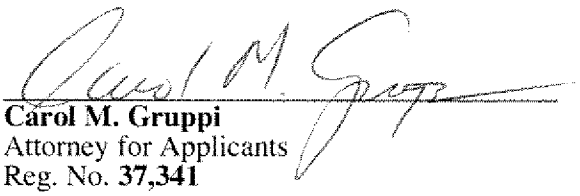

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